Citation:

He J, Gu D, Wu X, Chen J, Duan X, Chen J, Whelton PK. Effect of soybean protein on blood pressure: A randomized, controlled trial. *Ann Int Med.* 2005; 143: 1-9.

PubMed ID: 15998749

Study Design:

Randomized controlled trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

A test of the effect of soybean protein supplementation on systolic and diastolic blood pressure among individuals with pre-hypertension or stage 1 hypertension in three samples of community residents in the People's Republic of China.

Inclusion Criteria:

Men and women 35 to 65 years of age, who had an average systolic blood pressure of 130mm to 159mm Hg, diastolic blood pressure of 80mm to 99mm Hg or both based on an average of nine readings (three readings on each of three visits).

Exclusion Criteria:

1. Self-reported use of anti-hypertensive medications in the previous two months
2. A history of cardiovascular disease, diabetes mellitus, cancer, chronic obsructive pulmonary disease, psychiatric disease or any other serious, life-threatening illness that required medical treatment
3. Serum creatinine level of 150.3umol per L or greater (at least 1.7mg per dL) at screening examination; or alcohol intake of 21 drinks or more per week or at least 40g per day
4. Pregnant women or women who intended to become pregnant during the study.

Description of Study Protocol:

Recruitment

At community-based blood pressure pre-screening.

Design

- Random allocation of 150 study participants to receive soybean protein supplementation and 152 controls
- The study group received 40g of isolated soy protein supplement per day in cookies for 12

weeks
- Controls received similar cookies with 40g of complex carbohydrate
- Cookies were substituted for one meal daily for 12 weeks
- Blood pressure readings were taken at six and 12 weeks.

Blinding Used

- Double-blind
- Participants were randomized using a computer-generated series number, which was sealed in an envelope
- Randomization was known only to the study coordinator; all other investigators and data collectors were blinded to the group assignment.

Intervention

- The study group received 40g of isolated soy protein supplement per day in cookies for 12 weeks
- Controls received similar cookies with 40g complex carbohydrate
- Cookies were substituted for one meal daily for 12 weeks.

Statistical Analysis

- Trial was designed to provide more than 80% statistical power to detect a three-mm Hg reduction in SBP and a two-mm Hg reduction in DBP
- Differences between baseline and follow-up measurements examined using Student's T-tests
- Linear regression models were used to estimate the net difference in BP and SE adjustment for the clinical centers.

Data Collection Summary:

Timing of Measurements

Baseline, six and 12 weeks.

Dependent Variables

- Urinary sodium and potassium in mmol per day from urine collection
- Body weight in kg measured on a scale
- Systolic blood pressure measured three times by a trained technician
- Diastolic blood pressure measured three times by a trained technician.

Independent Variables

- Soy protein intake (40g per day)
- Energy, protein, carbohydrate, fat, saturated fat, polyunsaturated fat assessed by dietary recall.

Description of Actual Data Sample:

Initial N

- 302 subjects

- 150 in the experimental group (51.3% women)
- 152 in the control group (55.3% women).

Attrition (final N)

- 139 in the experimental group
- 137 in control group.

Age

- *Experimental group mean:* 50.8±9.3
- *Control group mean:* 51.4±9.2.

Ethnicity

Chinese.

Anthropometrics

- Body mass index and waist circumference were similar at baseline between groups
- Percentage with BMI of at least 25kg/m^2 was 76 in the intervention group and 69.7 in the control group.

Location

Three centers in Beijing and Wuhan, China.

Summary of Results:

Variables	Soybean Protein Group	Complex Carbohydrate Control Group Measures and Confidence Intervals	Statistical Significance of Group Difference P-Value+
Energy, kcal			
Baseline	2,334±888	2,250±767	>0.2
Change in 6 weeks	32±731	27±675	>0.2
Change in 12 weeks	24±725	32±752	>0.2
Protein,g			
Baseline	69.7±28.5	68.7±31.0	>0.2
Change in 6 weeks	25.9±27.9	-1.3±27.6	<0.001
Change in 12 weeks	26.3±31.7	-1.3±35.2	<0.001
Carbohydrate, g			
Baseline	311.2 ±103.4	306.9±96.6	>0.2
Change in 6 weeks	-9.7±99.1	20.4±94.2	0.01
Change in 12 weeks	-8.3±95.4	16.2±97.6	0.04
Fat, g			

Baseline	86.1±53.0	80.9±45.3	>0.2
Change in 6 weeks	-3.6±46.5	-4.1±46.3	>0.2
Change in 12 weeks	-5.2±47.2	-4.9±48.1	>0.2
Saturated fat, g			
Baseline	21.1±14.8	20.0±12.8	>0.2
Change in 6 weeks	-2.2±16.6	-1.6±16.5	>0.2
Change in 12 weeks	-2.5±18.4	-2.5±16.8	>0.2
Polyunsaturated fat, g			
Baseline	26.5±18.0	25.7±18.5	>0.2
Change in 6 weeks	2.2±17.1	1.6±20.9	>0.2
Change in 12 weeks	1.6±20.1	1.3±19.2	>0.2
Urinary sodium, mmol/d			
Baseline	188.3±74.8	187.6±70.7	>0.2
Change in 6 weeks	-7.0±90.7	-5.5±85.1	>0.2
Change in 12 weeks	-7.6±100.9	-9.3±91.9	>0.2
Urinary potassium, mmol/d			
Baseline	32.9±14.0	33.7±12.3	>0.2
Change in 6 weeks	5.6+22.1	5.4±21.3	>0.2
Change in 12 weeks	4.2±21.0	4.2±22.4	>0.2
Body weight, kg			
Baseline	70.6±11.1	70.0±10.6	>0.2
Change in 6 weeks	0.51±2.67	0.18±1.43	0.19
Change in 12 weeks	0.36±2.81	0.04±2.54	>0.2

Other Findings

- Compared with the control group, the net changes in SBP and DBP were -4.31mm Hg (95% CI: -2.11mm to -6.51mm Hg, P<0.001) and -2.76mm Hg (CI: -1.35mm to -4.16mm Hg, P<0.001), respectively, after the 12-week intervention
- The net changes in SBP and DBP reductions were -7.88mm Hg (95% CI: -4.66mm to -11.1mm Hg) and -5.27mm Hg (CI: -3.05 mm to -7.49mm Hg), respectively, in persons with HTN and -2.34mm Hg (CI: 0.48mm to -5.17mm Hg) and -1.28mm Hg (CI: 0.52mm to -3.07mm Hg), respectively, in those without HTN.

Author Conclusion:

- Soybean protein supplementation resulted in a reduction in systolic and diastolic blood pressure
- These findings suggest that increased intake of soybean protein may play an important role in preventing and treating hypertension.

Reviewer Comments:

- *Mean soy intake did not achieve the amounts desired by researchers, which may indicate the*

need to study intake of smaller amounts

- *This trial did not examine whether the BP reduction was due to protein or isoflavones in soybean.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No

	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes